

bonding a first nucleotide having at least one protected chemical functional group;
bonding a second nucleotide having at least one protected chemical functional group to a deprotect chemical functional group of the nucleotide bonded molecule or said other deprotected molecule, and

repeating the selective deprotection of a chemical functional group on a bonded protected nucleotide or a protected bonded molecule and the subsequent bonding of an additional nucleotide to said deprotected chemical functional group until at least two separate oligonucleotides of desired length are formed on the substrate surface.

Kindly cancel claims 45-46.

~~44~~ ~~47~~. (Twice Amended) A method for electrochemical placement of a material at a specific location on a porous substrate, which comprises the steps of:

providing a substrate having at its surface at least one electrode that is proximate to at least one molecule that is reactive with an electrochemically generated reagent,

placing a substrate having at its surface at least one electrode that is proximate to at least one molecule that is reactive with an electrochemically generated reagent, and further placing a buffering solution in contact with the electrode and the porous substrate to prevent electrochemically generated reagents from leaving the locality of the electrode, wherein a buffering solution is one having the capacity to prevent pH changes upon addition of small amounts of acids or bases,

applying a potential to said electrode sufficient to generate electrochemical reagents capable of reacting to the at least one molecule proximate to the electrode, and

producing a chemical reaction thereby.

Kindly cancel claim 48 in view of the amendment to claim 47.

REMARKS

Applicant respectfully requests reconsideration of the above-identified patent application in view of the foregoing amendment and following remarks. Applicant has amended claims 1 and 47 to add the limitation from claims 2 and 48, respectively regarding the buffering solution. In addition, in an effort to clarify the term "buffering solution", applicant has added a standard in the art definition of a buffer to claims 1, 16, 41 and 47. Applicant wants to make sure the use of the term "buffer" and its derivative terms (such as "buffering solution") are standard terms as used by chemists. For example, what would not be considered a buffer is a zwitterion (such as an amino acid solution) that has no buffering capacity. Claims 1, 18, 41 and 43 were amended to remove the notion of a scavenging solution. While applicant considers a scavenging solution to be a form of a buffering solution that provides for irreversible changes (as opposed to a reversible

equilibrium in a buffering solution), that subject matter is the subject of two issued sibling patents. Therefore, the removal of a scavenging solution was done to avoid overlapping subject matter. Claim 10 was canceled because it is redundant to claim 9. Claim 25 was canceled because it depends upon claim 24 that was previously canceled. Claims 45-46 were canceled because the subject matter of these claims is the subject of a pending priority patent application. No new matter has been added. Entry of the foregoing amendment is respectfully requested. Claims 1-9, 12-23, 26-44 and 47-51 are pending.

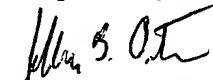
Double Patenting

The present pending claims were the subject of an obviousness-type double patenting rejection over claims 1-49 of related U.S. Patent 6,093,302 and the claims of USSN 09/394,138, now U.S. Patent 6,280,595. Applicant has cleaned up and clarified the claims of this patent application so that they are ready for issuance and not of identical scope of either the '302 Patent or the '595 Patent. Applicant is further providing a Terminal Disclaimer to address this rejection.

Accordingly, the present patent application is ready for issuance in view of the Terminal Disclaimer.

In view of the foregoing amendment and remarks, applicant respectfully requests withdrawal of the rejections, and allowance of pending claims 1-9, 12-23, 26-44 and 47-51.

Respectfully submitted,



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Clean copy of pending claims:

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1. A method for electrochemical placement of a material at a specific location on a porous substrate, which comprises the steps of:

providing a substrate having at its surface at least one electrode that is proximate to at least one molecule bearing at least one protected chemical functional group,

placing a buffering solution in contact with the electrode and the porous substrate to prevent electrochemically generated reagents from leaving the locality of the electrode, wherein a buffering solution is one having the capacity to prevent pH changes upon addition of small amounts of acids or bases,

applying a potential to said electrode sufficient to generate electrochemical reagents capable of deprotecting at least one of the protected chemical functional groups of said molecule, and

bonding the deprotected chemical functional group with a monomer or a pre-formed molecule.

3. A method according to claim 1, wherein said buffering solution is selected from acetate buffers, borate buffers, carbonate buffers, citrate buffers, glycine buffers, HEPES buffers, MOPS buffers, phosphate buffers, TRIS buffers and KI solutions.

4. A method according to claim 1, wherein said buffering solution is present in a concentration of at least 0.01 mM.

5. A method according to claim 1, wherein the concentration of the buffering solution ranges from 0.1 to 100 mM.

6. A method according to claim 1, wherein said monomer or preformed molecule has at least one other protected chemical functional group at a site different from where bonding with the deprotected chemical functional group of the molecule occurs.

7. A method according to claim 1, wherein said monomer is an amino acid.

8. A method according to claim 1, wherein said pre-formed molecule is selected from proteins, nucleic acids, polysaccharides, and porphyrins.

9. A method according to claim 1, wherein said molecule is a linker molecule or a monomer.

12. A method according to claim 1, wherein said protected chemical functional groups are protected with an acid or base labile protecting group.

13. A method according to claim 1, wherein said at least one electrode comprises an array of electrodes.

14. A method according to claim 13, wherein said array of electrodes comprises at least 100 electrodes.

15. A method according to claim 6, further comprising sequentially deprotecting the other protected chemical functional group of the monomer or pre-formed molecule and bonding to the deprotected monomer or pre-formed molecule another monomer or pre-formed molecule.

14 16. A method for electrochemical synthesis of an array of separately formed polymers on a porous substrate, which comprises the steps of:

placing a buffering solution in contact with an array of electrodes that is proximate to a substrate surface, said surface being proximate to one of more molecules bearing at least one protected chemical functional group attached thereto, wherein a buffering solution is one having the capacity to prevent pH changes upon addition of small amounts of acids or bases;

selectively deprotecting at least one protected chemical functional group on at least one of said molecules;

D2 bonding a first monomer having at least one protected chemical functional group to one or more deprotected chemical functional groups of said molecule;

selectively deprotecting a chemical functional group on the bonded molecule or another of said molecules bearing at least one protected chemical functional group;

bonding a second monomer having at least one protected chemical functional group to a deprotected chemical functional group of the bonded molecule or said other deprotected molecule; and

repeating the selective deprotection of a chemical functional group on a bonded protected monomer or a bonded protected molecule and the subsequent bonding of an additional monomer to said deprotected chemical functional group until at least two separate polymers of desired length are formed on the substrate surface.

17. A method according to claim 16, wherein during said selective deprotection steps, the electric potential is applied to one or more selected electrodes sufficient to generate electrochemical reagents at the selected electrodes capable of deprotecting the chemical functional groups on said proximate molecules or monomers.

D3 16 18. A method according to claim 16, wherein said buffering solution prevents the electrochemical reagents generated at selected electrodes from deprotecting the chemical functional groups of molecules or monomers proximate to the unselected electrodes.

19. A method according to claim 16, wherein said buffering solution is selected from acetate buffers, borate buffers, carbonate buffers, citrate buffers, glycine buffers, HEPES buffers, MOPS buffers, phosphate buffers, TRIS buffers and KI solutions.

20. A method according to claim 16, wherein said buffering solution is present in a concentration of at least 0.01 mM.

21. A method according to claim 16, wherein the concentration of the buffering solution ranges from 0.1 to 100 mM.

22. A method according to claim 16, wherein said monomers are amino acids.
23. A method according to claim 16, wherein said molecules are linker molecules or monomers.
26. A method according to claim 23, wherein said linker molecule comprises a group cleavable by an electrochemically generated reagent, which cleavable group enables removal from said substrate of one or more bonded molecules.
27. A method according to claim 16, wherein said protected chemical functional groups are protected with an acid or base labile protecting group.
28. A method according to claim 16, wherein said substrate is formed from at least one material selected from undoped semiconductor, glass, ceramics, polymers, and waxes.
29. A method according to claim 16, wherein said array of electrodes comprises at least 100 electrodes.
30. A method according to claim 16, wherein said array of electrodes comprises at least 2048 electrodes.
31. A method according to claim 30, wherein said array of electrodes comprises at least 204,800 electrodes.
32. A method according to claim 16, wherein each of the electrodes in said array ranges in diameter from less than 1 micron to about 100 microns.
33. A method according to claim 16, wherein the electrodes of said array are formed from platinum or palladium.
34. A method according to claim 33, wherein said platinum or palladium electrodes are preloaded with hydrogen.
35. A method according to claim 16, which further comprises a capping step wherein unbonded deprotected chemical functional groups on said molecules or monomers are capped with acetic anhydride or n-methylimidazole.
36. A method according to claim 16, which further comprises an additional bonding step wherein a pre-formed molecule is bonded to a deprotected chemical functional group on one or more of said molecules or monomers.
37. A method according to claim 36, wherein said pre-formed molecule is selected from proteins, nucleic acids, polysaccharides, and porphyrins.
38. A method according to claim 36, wherein said pre-formed molecule bears at least one protected chemical functional group to which an additional monomer may bond following selected deprotection of the chemical functional group on the pre-formed molecule.
39. A method according to claim 17, wherein the one or more selected electrodes to which an electric potential is applied are selected by a switching mechanism selected from

CMOS switching circuitry, radio frequency addressable switches, microwave frequency addressable switches, and light addressable switches.

40. A method according to claim 16, wherein said array of electrodes comprises at least 1024 electrodes.

37 41. A method for electrochemical synthesis of an array of separately formed oligonucleotides on a porous substrate, which comprises the steps of:

placing a buffering solution in contact with an array of electrodes that is proximate to a substrate surface, said surface being proximate to one of more molecules bearing at least one protected chemical functional group attached thereto, wherein a buffering solution is one having the capacity to prevent pH changes upon addition of small amounts of acids or bases;

selectively deprotecting at least one protected chemical functional group on at least one of said molecules;

bonding a first nucleotide having at least one protected chemical functional group;

D4 bonding a second nucleotide having at least one protected chemical functional group to a deprotect chemical functional group of the nucleotide bonded molecule or said other deprotected molecule, and

repeating the selective deprotection of a chemical functional group on a bonded protected nucleotide or a protected bonded molecule and the subsequent bonding of an additional nucleotide to said deprotected chemical functional group until at least two separate oligonucleotides of desired length are formed on the substrate surface.

42. A method according to claim 41, wherein during said selective deprotection steps, an electric potential is applied to one or more selected electrodes sufficient to generate electrochemical reagents at the selected electrodes capable of deprotecting the chemical functional groups on said proximate molecules or nucleic acids.

D5 39 43. A method according to claim 41, wherein said buffering solution prevents the electrochemical reagents generated at selected electrodes from deprotecting the chemical functional groups or molecules or nucleotides proximate to unselected electrodes.

44. A method according to claim 8, wherein said preformed molecule is a nucleic acid.

41 47. A method for electrochemical placement of a material at a specific location on a porous substrate, which comprises the steps of:

D6 providing a substrate having at its surface at least one electrode that is proximate to at least one molecule that is reactive with an electrochemically generated reagent,

placing a substrate having at its surface at least one electrode that is proximate to at least one molecule that is reactive with an electrochemically generated reagent, and further placing a buffering solution in contact with the electrode and the porous substrate to prevent electrochemically generated reagents from leaving the locality of the electrode, wherein a

buffering solution is one having the capacity to prevent pH changes upon addition of small amounts of acids or bases,

applying a potential to said electrode sufficient to generate electrochemical reagents capable of reacting to the at least one molecule proximate to the electrode, and producing a chemical reaction thereby.

49. A method according to claim 48, wherein said buffering solution is selected from acetate buffers, borate buffers, carbonate buffers, citrate buffers, glycine buffers, HEPES buffers, MOPS buffers, phosphate buffers, TRIS buffers and KI solutions.

50. A method according to claim 48, wherein said buffering solution is present in a concentration of at least 0.01 mM.

51. A method according to claim 48, wherein the concentration of the buffering solution ranges from 0.1 to 100 mM.